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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/881,823	06/15/2001	Wenyuan Shi	22851-032	8957

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EXAMINER
ZEMAN, ROBERT A

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/881,823	SHI ET AL.	
	Examiner	**Art Unit**	
	Robert A. Zeman	1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 30 June 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *04 July 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☒ The proposed amendment(s) will not be entered because:

(a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☒ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: *see attached*.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attached*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *none*.

Claim(s) objected to: *none*.

Claim(s) rejected: *25-53*.

Claim(s) withdrawn from consideration: *5-8, 11-14, 18-24*.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

ADVISORY ACTION

The amendment filed 6-30-2004 under 37 CFR 1.116 in reply to the final rejection has been considered but is not deemed to place the application in condition for allowance and will not be entered because:

The proposed amendment raises new issues that would require further consideration and/or search.

The proposed amendment raises the issue of new matter.

Claims 5-8, 11-14 and 18-53 are pending. Claims 5-8, 11-14 and 18-24 are withdrawn from consideration. Claims 25-53 are currently under examination.

Claim Rejections Maintained

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional rejection of claims 25, 35 and 37-38 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 7, 10, 12 and 17 of

copending Application No. 09/378,577 is maintained for reasons of record. Applicant has stated they will not comment on the merit of said rejection until any of the claims at issue in the copending application have been allowed. Consequently, in the absence of any rebuttal the rejection is maintained for the reasons set forth in the previous Office action.

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The new matter rejection of claims 25-53 under 35 U.S.C. 112, first paragraph, is maintained for reasons of record.

Applicant argues:

1. The phrase "wherein the portion of the monoclonal antibody that triggers the humoral immune response is from the same species as the subject" constitutes a rephrasing of a passage within the specification.

2. The specification (page 4, lines 3-18) disclose that antibodies to treat dental caries must be recognized by the human immune system and should be humanized in order to elicit the desired cytotoxic effect of antibody binding in humans.

Applicant's arguments have been fully considered and deemed to be non-persuasive. The cited passages do not support the fully scope of the rejected claims. The passage on page 3 (lines 18-25) is limited to IgG and IgM antibodies. Moreover, contrary to Applicant's assertion, the

specification does not disclose on page 4 (lines 3-18) that antibodies are humanized in order to elicit a cytotoxic effect. Chimeric antibodies are humanized in order to reduce the antigenicity of said antibodies. Moreover, Applicant is reminded that the instant claims read on a broader genus than humanized antibodies.

The rejection of claims 25-53 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for reasons of record.

Applicant argues:

1. A humoral immune response to an antigen can be triggered by the constant region of the antibody to the antigen.

2. Exhibit B shows that humanized mouse SWLA antibodies can bind to the Fc receptors on human lymphocytes and trigger the destructive effects of the humoral immune response using the immune components present in saliva.

Applicant's arguments have been fully considered and deemed non-persuasive.

Contrary to Applicant's assertion, the data disclosed in Exhibits B1 and B2 do not demonstrate that the humanized mouse SWLA antibodies can trigger a humoral immune response. All "experiments" were done in the presence of *S. mutans*. It is the antigens on the bacteria that "trigger" the humoral immune response not the chimeric antibodies. Consequently, the rejection is considered valid and is maintained for the reasons of record and reiterated below.

The amended claims are drawn to methods of treating or preventing dental caries comprising the administration of a chimeric antibody wherein the chimeric antibody must

possess four properties. Said chimeric antibodies must 1) bind to a cariogenic organism; 2) elicit a humoral immune response in the oral cavity to an antigen of the cariogenic organism; 3) the portion of the chimeric antibody that binds to the cariogenic organism must be derived from a species other than that of the treated subject; and 3) the portion of the chimeric monoclonal antibody that triggers the humoral immune response must be derived from the same species as the subject.

The humoral branch of the immune system involves the interaction of B cells with antigen and their subsequent proliferation of and differentiation into antibody-secreting plasma cells. Therefore the "trigger" for **any** humoral immune response is the interaction of the antigen with B cells. The chimeric antibodies of the instant invention, by definition, cannot trigger a humoral immune response to an antigen of the cariogenic organism since any antibody produced as a result of them being the "trigger" would result in antibodies with specificity for the chimeric antibodies not the cariogenic organism. As illustrated by the 2nd Edition of Immunology (W.H. Freeman and Company, 1994, pages 19-20), the humoral response begins when antigen cross-links the membrane bound antibody molecules on a B cell and the B cell interacts with an antigen-specific T_H cell. After processing the antigen the B cell presents it along with a class II MHC molecule on its membrane. The antigen-specific T_H cell binds to this antigen-MHC complex and begins to secrete cytokines that serve to stimulate B cell division and differentiation resulting in a population of antibody-secreting plasma cells and memory cells. Since the instant invention is drawn to methods of treating dental caries wherein the application of the claimed chimeric antibody **elicits** a humoral immune response. This means that the treated subject's B cells bind to the chimeric antibody (which serves as the antigen) resulting in the production of

antibodies with specificity for the chimeric antibody (anti-idiotype antibodies). The specification provides no guidance on what type of chimeric antibodies, if any, would be effective in treating dental caries in such an anti-idiotypic manner. Moreover, the instant claims are internally inconsistent. The instant claims require that the Fab portion of the chimeric antibody (the part that binds the cariogenic organism) be derived from a species other than that of the treated subject and that the portion of the chimeric antibody that that triggers the humoral response (i.e. the portion of the chimeric that binds to the B cell) be derived from a species other than that of the treated subject. These two limitations are contradictory since the Fab portion of the chimeric antibody not only binds the cariogenic organism but also "triggers" the humoral response. Moreover, that latter limitation encompasses the production of autoantibodies that is usually deleterious to the subject producing them. While the skill in the art of immunology is high, one of skill in the art would not be able to make a chimeric antibody to be used in the claimed method that would meet all the limitation of the rejected claims. It should also be noted that in the humoral arm of the immune system, antibodies serve as effectors of the humoral response by binding to antigen or neutralizing it or facilitating its elimination via cross-linking the antigen on a microorganism (resulting in clusters more easily ingested by phagocytic cells) or by activating the complement system (which results in the lysis of said microorganism).

Conclusion

No claim is allowed.

Applicant is reminded that the art rejections were withdrawn in light of the amendment filed on 10-7-2003. Said amendments have been deemed to constitute new matter. If the new matter is resolved, the previously made art rejections may be reinstated.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert A. Zeman
September 2, 2004

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